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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,700	07/07/2005	Jorg Bewersdorf	21295.0109US1 (E0673US)	4035

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EXAMINER

LYONS, MICHAEL A

ART UNIT	PAPER NUMBER
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2877

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/541,700

Applicant(s)

BEWERSDORF ET AL.

Examiner

Michael A. Lyons

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>070705 and 061606</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

The abstract of the disclosure is objected to for the reasons set forth below. Correction is required. See MPEP § 608.01(b).

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The disclosure is objected to because of the following informalities: the disclosure fails to make reference to the claimed priority documents (either the PCT International application or the prior foreign application as indicated on the declaration), and the disclosure fails to use any headings to separate sections of the disclosure, making it difficult for the examiner to ascertain when the disclosure refers to prior art and background information, or when the disclosure refers to the instant invention.

Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without

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underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Objections

Claims 5 and 17 are objected to because of the following informalities: the word Forster is misspelled "Foerster" in both claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims (1-23) are all generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. These grammatical and idiomatic errors make it difficult for the examiner to ascertain what the applicants' claim to be their invention. As such, the rejections below under 35 USC 102 and 35 USC 103 are a treatment of the claims as best understood by the examiner, and the examiner requests that applicants review all pending claims to ensure conformity with current U.S. practice and correct all grammatical and idiomatic errors that make the claims confusing.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 4 recites the broad recitation multiple-photon excitation, and the claim also recites particularly by two-photon excitation, which is the narrower statement of the range/limitation.

As for claim 6, the claim states, "The illumination light exhibits a further illumination wavelength, and occurs via a virtual or via a real intermediate level". What occurs via a virtual or via a real intermediate level? For purposes of examination, the examiner assumes that excitation of the molecules in the sample is what occurs here, in accordance with similar claim 19.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 7 recites the broad recitation a higher excitation level, and the claim also recites in particular via an S₀-S₂ transition, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex*

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parte Wu, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 8 recites the broad recitation in a range of 0.5 to 0.9, and the claim also recites in particular in a range of 0.6 to 0.8, in particular 0.75, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 10 recites the broad recitation diameter is set smaller than 1 Airy disc, and the claim also recites in particularly 0.7 to 0.8 Airy discs, in particular 0.7 Airy discs, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 13 recites the broad recitation a phase plate that comprises in particular regions of varying phase delay, and the claim also recites in particular a $\lambda/2$ plate, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

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USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 17 recites the broad recitation the light source is a laser, and the claim also recites particularly a pulse laser, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 17 recites the broad recitation multiple-photon excitation, and the claim also recites particularly by two-photon excitation, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is

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followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 20 recites the broad recitation excitation occurs via a higher excitation level, and the claim also recites particularly via an S₀-S₂ transition, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 21 recites the broad recitation the illumination wavelength to detection wavelength ratio lies in a range between 0.5 and 0.9, and the claim also recites in particular in a between range 0.6 to 0.8, in particular 0.75, which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 23 recites the broad recitation having an aperture diameter smaller than 1 Airy disc, and the claim also recites in particular 0.7 to 0.8 Airy discs, in particular 0.7 Airy discs, which is the narrower statement of the range/limitation.

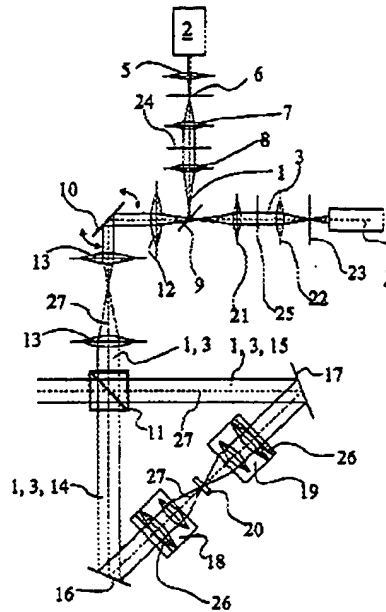
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, and 11-16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gugel et al (US 2002/0109913), as best understood by the examiner.



Regarding claim 1, Gugel (Fig. 1) discloses a method for confocal 4-pi microscopy, comprising coherently illuminating with light source 2 a sample 20 from two sides via one objective 18, 19 for each side of the sample with illumination light that has at least one illumination wavelength, whereby a stationary illumination wave with one main illumination maximum and with secondary illumination maxima is produced by interference of the illumination light in the sample (see paragraph 0004, for example), and detecting using detector 4 the detection light emitted by the sample that exhibits at least one detection wavelength, this light passing through the two objectives 18, 19, where the detection light is made to interfere, thereby producing in the sample a detection pattern with one main detection maximum and with secondary detection maxima produced such that the secondary illumination maxima and the secondary detection maxima are located in different places (see paragraph 0004, for example, and paragraphs 0035-0038 for a description of the apparatus and corresponding method contained in Fig. 1 set forth above).

As for claim 2, Gugel discloses that the objectives exhibit a pupil, with the position of the secondary illumination and detection maxima able to be changed via the introduction of pupil filters on at least one pupil plane (see paragraph 0021).

As for claim 3, Gugel discloses that sample 20 “is a biological specimen that has been specifically labeled with fluorescent dyes” (paragraph 0036).

Regarding claim 11, Gugel (Fig. 1) discloses a confocal 4-pi microscope comprising a light source 2 that generates an illumination light that exhibits at least one illumination wavelength, which is directable via optical elements set forth in Fig. 1 from two sides by one objective 18, 19 each onto a sample 20, in which a stationary illumination wave having a main illumination maximum and secondary illumination maxima is produced by interference of the illumination light in the sample (see paragraph 0004, for example) and a detector 4 that detects detection light emitted by the sample that passes through both objectives and that exhibits at least one detection wavelength, characterized in that the detection light interferes and a detection pattern is produced in the sample with a main detection maximum and with secondary detection maxima, whereby the secondary illumination maxima and the secondary detection maxima are located at different places (see paragraph 0004, for example, and also see paragraphs 0035-0038 for a description of the apparatus and corresponding method contained in Fig. 1 set forth above).

As for claim 12, Gugel discloses that the objectives exhibit a pupil, with the position of the secondary illumination and detection maxima able to be changed via the introduction of pupil filters on at least one pupil plane (see paragraph 0021).

As for claim 13, Gugel discloses that phase plates can serve as a type of optical component for the pupil filter, of which $\lambda/2$ plates are a specific type (paragraph 0022).

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As for claim 14, the detector of Gugel is inherently set to a detection wavelength to ensure proper operation of the detector, enabling full detection of the interference pattern striking the detector.

As for claim 15, Gugel discloses, "The illuminating light of suitable wavelength excites the fluorescent dyes to fluoresce". (paragraph 0036).

As for claim 16, Gugel discloses that sample 20 "is a biological specimen that has been specifically labeled with fluorescent dyes" (paragraph 0036).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gugel et al (US 2002/0109913) in view of Denk et al (EP 0807814), as best understood by the examiner.

As for claims 4 and 17, Gugel discloses the claimed invention as set forth above regarding claims 1, 3, 11, and 16, but fails to disclose the excitation of the sample being accomplished by multiple-photon excitation, particularly by two-photon excitation.

Denk, however, discloses a method for molecular excitation where two-photon molecular excitation of fluorescence in laser scanning microscopy occurs (page 2, lines 51-52).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to perform two-photon molecular excitation of the sample of Gugel as per Denk, the motivation being that two-photon molecular excitation “provides improved background discrimination, reduces photobleaching of the fluorophores, and minimizes the photo damage to living cell specimens” (page 3, lines 9-17).

Claims 5 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gugel et al (US 2002/0109913) in view of Engelhardt et al (US 2002/027709), as best understood by the examiner.

As for claims 5 and 18, Gugel discloses the claimed invention as set forth above regarding claims 1, 3, 11, and 16, but fails to disclose the excitation of the sample comprising a Forster-resonant energy transfer (FRET) within the sample.

Engelhardt, however, discloses excitation of a sample using FRET (paragraph 0006).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use FRET to excite the sample of Gugel as per Englehardt, the motivation being that FRET merely involves optically exciting molecules from one excitation state to another in order to acquire an image of the excited molecule at a wavelength different from the excitation wavelength used to illuminate the molecule.

Claims 6-10 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gugel et al (US 2002/0109913), as best understood by the examiner.

As for claims 6 and 19, Gugel discloses the claimed invention as set forth above regarding claims 1, 3, 11, and 16, but fails to disclose the illumination light exhibiting an illumination wavelength that causes excitation to occur via a virtual or via a real intermediate level.

Official Notice is taken, however, as to the excitation of molecules via a real intermediate level to be known in the art, and it would have been obvious to one having ordinary skill in the art at the time the invention was made to excite the molecules in the Gugel sample via a real intermediate level, the motivation being that the intermediate excitation level of a molecule is known based on the type of molecule being used, and knowing the real intermediate level allows for the excitation to be more optimally controlled, leading to more accurate results.

As for claims 7 and 20, Gugel discloses the claimed invention as set forth above regarding claims 1, 3, 11, and 16, but fails to disclose the excitation occurring via a higher excitation level, in particular via an S_0 - S_2 transition.

Official Notice is taken, however, as to the excitation of molecules via an S_0 - S_2 transition to be known in the art, and it would have been obvious to one having ordinary skill in the art at the time the invention was made to excite the molecules in the Gugel sample via a high excitation level, such as an S_0 - S_2 transition, the motivation being that the S_0 - S_2 transition for a molecule is known based on the type of molecule being used, and knowing the S_0 - S_2 transition allows for the excitation to be more optimally controlled, leading to more accurate results.

As for claims 8 and 21, Gugel discloses the claimed invention as set forth above regarding claims 1 and 11, but fails to disclose the illumination to detection wavelength ratio lying in a range between 0.5 and 0.9, in particular 0.75.

It would have been obvious, though, to one having ordinary skill in the art at the time the invention was made to obtain an illumination to detection wavelength ratio to be 0.75, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this instance, the illumination to detection wavelength ratio will always be smaller than 1; the emission (detection) wavelength of an excited molecule will always be greater than the wavelength of the excitation illumination; the excited molecule, when returning to its previous state, has to emit a higher wavelength than the excitation wavelength. Finding an optimal ratio merely ensures more accurate results.

As for claims 9 and 22, Gugel discloses the claimed invention as set forth above regarding claims 1, 3, 11, and 16, but fails to disclose the fluorescent dye exhibiting an excitation and emission region in the frequency regions claimed.

It would have been obvious, though, to one having ordinary skill in the art at the time the invention was made to set the illumination or detection wavelength to the corresponding high or low frequency portion of the excitation region and/or the emission region, respectively, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

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As for claims 10 and 23, Gugel discloses the claimed invention as set forth above regarding claims 1 and 11, and discloses detection pinhole 6, but fails to disclose the diameter of the aperture of the pinhole.

However, it would have been an obvious matter of design choice to set the pinhole diameter to be 0.7 Airy discs in size, since such a modification would have involved a mere change in the size of a component. A change in size is generally recognized as being within the level of ordinary skill in the art. *In re Rose*, 105 USPQ 237 (CCPA 1955).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Pat. 6,552,795 to Bewersdorf.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael A. Lyons whose telephone number is 571-272-2420. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gregory J. Toatley can be reached on 571-272-2800 ext. 77. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

A handwritten signature in black ink, appearing to read "Michael A. Lyons", followed by a large, stylized, horizontal oval flourish.

Michael A. Lyons
Patent Examiner
March 13, 2007